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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,865	10/06/2003	Usha Kasid	224382	8115

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EXAMINER	
AEDER, SEAN E	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 05/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** *10/679,865*	**Applicant(s)** KASID ET AL.	
	Examiner Sean E. Aeder, Ph.D.	**Art Unit** 1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 20 April 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☐ The period for reply expires ______months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,7,8,10,36,38 and 42*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached pages .
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

After Final

The amendments to the claims and the Remarks/Arguments filed on 4/17/06 in response to the Final Rejection of 2/16/06 have been entered.

Claims 1, 7, 8, 10, 36, 36, 38, and 42 are pending.

Claims 1 and 36 have been amended by Applicant.

Claims 1, 7, 8, 10, 36, 36, 38, and 42 are currently under consideration.

Objection Withdrawn

The objection to claim 1 has been withdrawn in view of amendments.

Rejections Withdrawn

The rejection of claims 1, 7, 8, 10, 36, 38, and 42 under 35 U.S.C., first paragraph, as failing to comply with the written description requirement, is withdrawn in view of amendments.

The rejection of claims 1 and 7 under 35 U.S.C. 102(a), as being anticipated by Birren et al (Homo sapiens chromosome 11 clones RP11-85D24 map 11, 4/22/00), is withdrawn in view of amendments.

The rejection of claims 1, 7, 8, 10, 36, 38, and 42 under 35 U.S.C., second paragraph, for being indefinite, is withdrawn in view of amendments.

Response to Arguments

Claims 1, 7, 8, 10, 36, 38, and 42 remain rejected under 35 U.S.C., first paragraph, as failing to comply with the enablement requirement for the reasons of record and the reasons set-forth below.

The claims are broadly drawn to BRCC2 nucleic acids, vectors comprising said nucleic acids, and host cells comprising said vectors. The claims are further drawn to antisense oligonucleotides that inhibit the expression of said nucleic acids.

As stated in the Final Rejection of 2/16/06, the claims are not enabled because there is insufficient guidance and objective evidence that one of ordinary skill in the art would know how to predictably use the claimed invention in any substantial manner. The specification teaches uses for the claimed polynucleotide that rely on the unfounded assertion that BRCC2 is involved in a raf-1 apoptotic pathway. These uses include gene therapy (paragraph 92, in particular). Applicant has argued that the claimed polynucleotides can be used to produce BRCC2 protein which can be used as a therapeutic agent to generate antibodies. However, production of polypeptides with unknown functions to be used in a therapeutic for a "disease" (see paragraph 77, in particular) is not a credible utility. Further, without a correlation to a specific diseased state, using said polypeptides for the production of antibodies to be used to detect BRCC2 in patients (see paragraph 111, in particular) is not a substantial utility. Thus, Applicant is not enabled to use the claimed polynucleotides in any substantial manner. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polynucleotide and fragments thereof. Thus, *the previous Office Action have stated that there is no credible enablement for any substantial or well-established utility for the claimed polynucleotides*.

In the response filed 4/17/06, Applicants point-out that the present application contains data demonstrating that treatment of human breast cancer cells with a novel antisense raf oligonucleotide decreases expression of BCC2 gene (Figure 5). Further, Applicant states that inhibition of gene expression has been used to successfully show the involvement of other molecules in raf pathways. Applicant's data, along with information discussed in the background section of the specification, led Applicant to conclude that the BRCC2 gene is involved in a raf apoptotic pathway. Applicant also cites Riedel et al. (Eur. J. Immunol., 23, 3146-3150, 1993) and states that such techniques have been used to identify IL-2 as a molecule involved in the raf pathway. Applicant further cites *In re Brana*, 34 U.S.P.Q. 2d 1436, 1440 (Fed. Cir. 1995) and states "the applicant favorably compared their inventive compounds to similar known compounds, and concluded that since the known compounds were effective in treating cancer, the claimed compounds would be also. The court held that this comparison was sufficient to disclose a specific utility for the claimed compounds. Id. In this case, a utility for the inventive polynucleotide, namely that it is involved in a raf pathway related to cancer, was clearly asserted". Applicant further states that the examiner has failed to present any evidence whatsoever that suggests BRCC2 is not involved in a raf apoptotic pathway. Applicant further cites the MPEP: "A specification or disclosure which contains a teaching of the manner and process of making and using an invention...must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support"" MPEP 2164.04. "[T]he PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure." In re Brana, 34 U.S.P.Q. 2d at 1441. Applicants conclude this argument by stating "...Examiner has not presented any references which call into question the usefulness of the claimed invention. Furthermore, there is nothing about Applicant's invention alone that would cause one of skill in the art to doubt its usefulness as described in the specification. Indeed, it is not unreasonable to propose a treatment for cancer involving gene or protein. See id. A conclusory statement that the claimed invention is not involved in a raf pathway is insufficient to render the claimed invention useless. The Examiner failed to meet the required burden to support a prima facie case of lack of enablement...".

The arguments found in the Response filed 4/17/06 have been carefully considered but are deemed not to be persuasive. As indicated in the previous Office Actions, Applicant is not enabled to use the claimed polynucleotides in *any* substantial manner. Applicant relies on data demonstrating that inhibiting raf expression resulted in a decrease in expression of the claimed polynucleotides. Applicant then cites Riedel et al. and states that "such techniques have been used to identify IL-2 as a molecule involved in the raf pathway". Then, upon citing *In re Brana*, indicates that because the claimed polynucleotides were identified by a similar technique used to identify IL-2 as a molecule involved in a raf pathway, Applicant indicates that the claimed polynucleotides can be used in manners similar to those that use IL-2 or that the claimed polynucleotides are involved in a raf pathway related to cancer. However, the teaching of Riedel et al do not identify IL-2 as a member of the raf signaling pathway in a manner similar to the way Applicant identified an association between raf expression and BRCC2 expression. Riedel et al do not inhibit the expression of one polypeptide and conclude that inhibition of a second polypeptide demonstrates that both polypeptides are involved in a similar signaling pathway. Rather, Riedel et al clearly teaches that inhibition of raf expression inhibits IL-2 mediated proliferation (Figure 1, in particular). Combined with previous studies teaching IL-2 mediates raf phosphorylation (page 3146, in particular), the teachings of Riedel et al clearly indicate that raf lies downstream of IL-2 in a pathway regulating cell proliferation. These teachings of Riedel et al do not support that the claimed polynucleotides are involved in an IL-2 mediated proliferation pathway or that the claimed polynucleotides can be used in any substantial manner. Further, one of skill in the art would not conclude that the claimed polynucleotides share any functional or structural characteristics with IL-2. Thus, the claimed polynucleotides and polynucleotides of IL-2 are not "similar known compounds". Further, Examiner is not suggesting that the claimed polynucleotides are not involved in *any* raf pathway; however, Examiner is stating that the claimed polynucleotides cannot be used in any substantial manner with an expectation of success. Further, there is substantial reasoning to doubt the truth of a statement to the contrary. One of skill in the art would recognized that a concomitant decrease in expression of a novel polynucleotide, such as BRCC2, upon decreasing the expression of a polynucleotide which is enabled to be used in a substantial manner, such as raf, does not indicate that one is enabled to use both polynucleotides in a substantial manner. For instance, the teachings of Patel et al (Molecular Medicine, 1997, 3(10):674-685) clearly demonstrate that inhibition of Raf expression leads to the an increase in KAS-110 and KAS-111 gene expression (page 679, in particular). Further, Patel et al teaches that KAS-110 and KAS-111 are housekeeping genes that are expressed in most normal tissues and several cancer cell tissues (Figure 5 in particular). Thus, Patel et al concludes that Raf modulates the expression of genes with housekeeping functions (page 674, in particular). Therefore, there is no reason to believe that the claimed polynucleotides are not housekeeping genes. One of skill in the art would recognize that housekeeping genes do not have substantial utility. To obviate this rejection, it is suggested that Applicant demonstrate that the claimed polynucleotides would function in a method with substantial utility that was proposed upon filing of the application.

Claims 36 and 38 remain rejected under 35 U.S.C. 102(a), as being anticipated by Birren et al (Homo sapiens chromosome 11 cones RP11-85D24 map 11, 4/22/00) for the reasons of record and for the reasons set-forth below.

Claim 36 is drawn to an agent that inhibits the expression of a polynucleotide encoding the amino acid sequence of SEQ ID NO:2. Claim 38 is drawn to an agent of claim 36, which is an antisense oligonucleotide.

As stated in previous office actions, Birren et al teaches a polynucleotide sequence which encodes a polypeptide sequence >99% identical to instant SEQ ID

NO:2. Further, one of skill in the art anticipates a complementary sequence to a given SEQ ID NO. Thus, one of skill in the art anticipates a complementary polynucleotide sequence to one which encodes a polypeptide sequence >99% identical to instant SEQ ID NO:2. Further, the complementary polynucleotide of the polynucleotide taught by Birren et al would function as an antisense polynucleotide that would inhibit the expression of a polynucleotide encoding the amino acid sequence of instant SEQ ID NO:2.

In the response filed 4/17/06, Applicant amended claim 1 to recite "...a polynucleotide encoding the sequence of SEQ ID NO:2..." or its polynucleotide complement. Applicant argues that the Birren publication does not disclose such a polynucleotide.

The amendments to the claims and the arguments found in the Response filed 4/17/06 have been carefully considered but are deemed not to be persuasive. Although the amendments to the claims resulted in withdrawal of this rejection for claims 1 and 7, the amendments and the arguments did not address and do not overcome the rejection of claims 36 and 38. For the reasons stated above, the sequence taught by the Birren publication anticipate an antisense polynucleotide that would inhibit the expression of a polynucleotide encoding the amino acid sequence of instant SEQ ID NO:2.

Summary

No claim is allowed. Claims 1, 7, 8, 10, and 42 are rejected under 35 U.S.C. 112, first paragraph, but free of the prior art teaching a polynucleotide encoding the amino acid sequence of SEQ ID NO:2 or its polynucleotide complement. The closest prior art for claims 1, 7, 8, 10, and 42 is Birren et al (Homo sapiens chromosome 11 cones RP11-85D24 map 11, 4/22/00); however, Birren et al teaches a polynucleotide sequence which encodes a polypeptide sequence >99% identical to instant SEQ ID NO:2 and does not teach or suggest a polynucleotide sequence that is 100% identical to instant SEQ ID NO:2 or its complement.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER